

Neurofeedback to reduce anhedonia and improve outcomes in opioid use disorder: a feasibility study.

Sarah Paprotna ¹, Sarah Lichenstein ², Sarah Yip ², Declan Barry ², Jitendra Awasthi ¹, Kymberly Young ³, Kathleen Garrison ², Michelle Hampson ¹

¹ *Department of Radiology and Biomedical Imaging, Yale University, New Haven, United States*

² *Department of Psychiatry, Yale University, New Haven, United States*

³ *Department of Psychiatry, University of Pittsburgh, Pittsburgh, United States*

Introduction

Anhedonia and nonspecific autobiographical memory recall are transdiagnostic clinical phenotypes shared among several psychopathologies, including depression and opioid-use disorder (OUD) [1-3]. Previous work has successfully used real-time fMRI neurofeedback (NF) to improve memory recall, reduce anhedonia, and decrease depressive symptoms in depressed populations by training them to upregulate amygdala activity while recalling positive autobiographical memories [4]. Given anhedonia's prevalence in substance use disorders broadly and its association with poorer clinical outcomes [5, 6], our primary aim is to evaluate whether leveraging this neurofeedback paradigm will be associated with reductions in anhedonia in participants with OUD. The paradigm will be adapted to specifically select non-substance related autobiographical memories to be used during neurofeedback training. We predict that individuals who receive neurofeedback will report lower levels of anhedonia, as assessed by the Snaith-Hamilton Pleasure Scale (SHAPS). In addition, we predict they will show increased ability to recall positive, non-substance related autobiographical memories, as assessed by the Autobiographical Memory Test (AMT). We will also collect several exploratory measures to investigate if our protocol can improve other aspects of well-being, such as mood, perceived meaning in life, opioid use, and drug craving. Our primary objective is to evaluate whether a previously successful depression NF protocol can be adapted to reduce anhedonia and improve autobiographical memory in subjects with OUD.

Methods

In this first-in-human feasibility trial, two subjects will participate in five sessions, including two neurofeedback scanning sessions, where they will be instructed to upregulate amygdala activity while recalling non-substance related, positive autobiographical memories, and three clinical sessions, where they will complete the Autobiographical Memory Test. Additional clinical and neuropsychological measures will be collected at all five sessions. Figure 1 shows the study timeline.

To evaluate our primary aim, we will collect the SHAPS at each session and evaluate how each participant's score changes throughout the experiment. Along with assessing reductions in anhedonia, we will administer measures of personal meaning (Meaning in Life Questionnaire and Purpose in Life - Short Form), mood (Profile of Mood States), and substance use behaviors (Structured Clinical Interview for DSM-5, Response to Addiction Recovery and Patient-Reported Outcomes Measurement Information System: Severity of Substance Use), along with Visual Analog Scale ratings of mood, craving, and/or meaning in life, to explore whether improvement in upregulation of amygdala during autobiographical memory recall moderates these key clinical features.

Results

We have implemented the amygdala training protocol developed by Dr. Kymberly Young's group [4] here at Yale and verified that feedback is running as expected by comparing the neurofeedback value shown to pilot subjects in online versus offline analysis for each of the four H blocks (Figure 2). We are fully approved to recruit subjects and expect to have feasibility data collected and analyzed to share at rtFIN 2026.

Conclusions

We are running this feasibility study to determine whether an existing depression NF protocol can reduce anhedonia and improve positive autobiographical memory recall in patients with OUD. Additionally, we will evaluate whether this training can impact perceived meaning in life, opioid use, and drug craving as assessed at one week and one month post-training. By taking an fMRI NF protocol that has demonstrated significance, adapting it to treat OUD, and evaluating its impacts on clinical and neuropsychological function, this work represents a novel approach to OUD treatment and has potential to improve quality of life for those struggling with problematic substance use.

Figures (optional, only if needed)



Figure 1: Study timeline. Subjects will participate in three clinical sessions (CS) (pre-NF, along with 1 and 4 weeks post-NF), and two neurofeedback sessions (NFS)

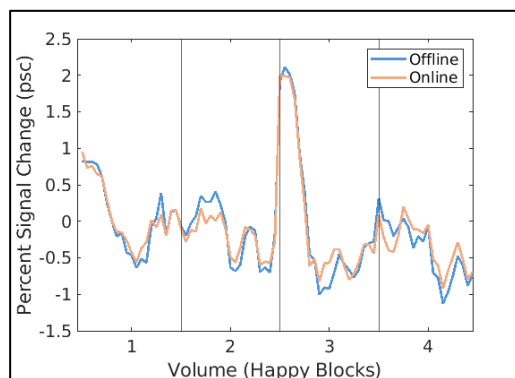


Figure 2: Value shown to pilot subjects in online versus offline analysis for each of the four H blocks. This analysis was used to validate the software we developed for providing feedback

References (optional, maximum 6)

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